

個案報告獎

Generalized tocilizumab hypersensitivity resolves after switching from subcutaneous to intravenous administration in rheumatoid arthritis.

類風濕性關節炎患者的全身性 Tocilizumab 過敏反應在皮下注射改為靜脈注射後緩解。

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Background

Tocilizumab (TCZ) is widely prescribed for rheumatoid arthritis (RA). Injection-site reactions (ISRs) are frequent with subcutaneous (SC) TCZ, whereas delayed hypersensitivity has been reported with intravenous (IV) infusion. We describe two patients whose generalized cutaneous hypersensitivity during SC therapy resolved after conversion to IV TCZ.

Case reports

Case 1

A 67-year-old woman with RA was switched to SC TCZ after inadequate response to etanercept, rituximab, and tofacitinib. At month 5 she developed generalized pruritic papules and eosinophilia; daily desloratadine and renewed glucocorticoids failed to prevent post-injection flares (Figure 1A). ISR appeared in month 7. Given sustained articular response, therapy was changed to IV TCZ, leading to gradual disappearance of urticaria and persistent remission for >30 months.

Case 2

A 78-year-old woman with destructive RA began SC TCZ after inadequate response to adalimumab and tofacitinib. Within two months she developed generalized eczematous eruptions with transient eosinophilia, recurring after each injection despite antihistamines and topical steroids (Figure 1B); ISR emerged in month 6. Switching to IV TCZ induced complete and durable remission for >18 months.

Discussion

IL-6 blockade can potentially skew immunity toward Th2. ISRs are common with SC tocilizumab, whereas generalized hypersensitivity reactions are rarely reported. To our knowledge, resolution of generalized hypersensitivity after an SC-to-IV switch has not been documented previously. Potential contributors include (1) protein aggregation in the concentrated SC formulation, (2) buffer-specific immunogenicity, and (3) charge-variant differences influencing immunogenicity. Thus, RA patients who respond to SC TCZ well but develop hypersensitivity may tolerate IV dosing better.

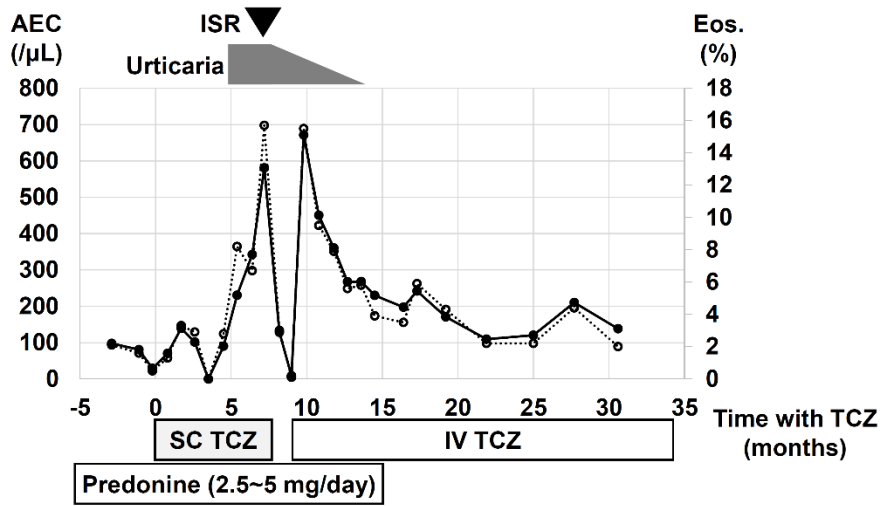
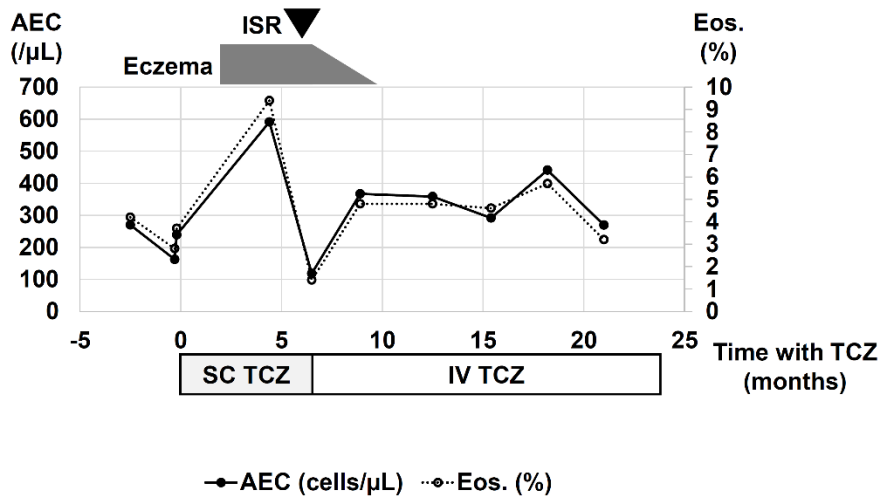
A**B**

Figure 1. Time course of eosinophil percentage (Eos. %), absolute eosinophil count (AEC), generalized cutaneous hypersensitivity, and injection-site reactions (ISRs) during subcutaneous (SC) and intravenous (IV) tocilizumab (TCZ) therapy in Case 1 (A) and Case 2 (B).

“Paradoxical inflammatory syndrome induced by Mycophenolate Mofetil in a patient with Systemic Lupus Erythematosus: A case report

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「霉酚酸酯引發的矛盾性炎症症候群於系統性紅斑狼瘡患者中的臨床報告」

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Abstract:

Mycophenolate mofetil (MMF) is a widely used immunosuppressive agent in systemic lupus erythematosus (SLE), particularly for lupus nephritis (LN). Although generally well tolerated, MMF can induce rare paradoxical inflammatory reactions, complicating diagnosis and treatment. We present the case of a 39-year-old woman with a 16-year history of SLE, who developed acute polyarthralgia with erythema and swelling in multiple joints shortly after initiating MMF therapy for LN. Laboratory tests revealed elevated C-reactive protein (CRP) and low complement levels, with no signs of infection. Symptoms worsened upon re-challenge with MMF and persisted despite switching to enteric-coated mycophenolate sodium (MPA). After discontinuing MMF/MPA, the patient's symptoms rapidly improved, and CRP levels decreased, confirming the diagnosis of MMF/MPA-induced inflammatory syndrome (Naranjo score = 9, indicating a definite adverse drug reaction). This case highlights the potential for MMF to induce paradoxical inflammation, mimicking disease flares or infections. The underlying mechanisms remain unclear but may involve the activation of proinflammatory cytokines, disruption of regulatory T-cells, or skewing of immune responses, such as promoting Th17 dominance. Notably, the reaction appears to be independent of the formulation, but rather intrinsic to MPA exposure itself as symptoms persisted with both MMF and MPA. Withdrawal of MMF/MPA resulted in rapid symptom resolution, avoiding unnecessary escalation of immunosuppressive therapy. Clinicians should maintain a high degree of suspicion when symptoms correlate with MMF initiation or dose adjustments, as misdiagnosis can lead to overtreatment. This case emphasizes the diagnostic challenge posed by paradoxical inflammatory reactions in autoimmune patients and underscores the importance of recognizing this rare adverse effect of MMF to prevent unnecessary immunosuppression.

The clinical course was depicted in **Figure 1**.

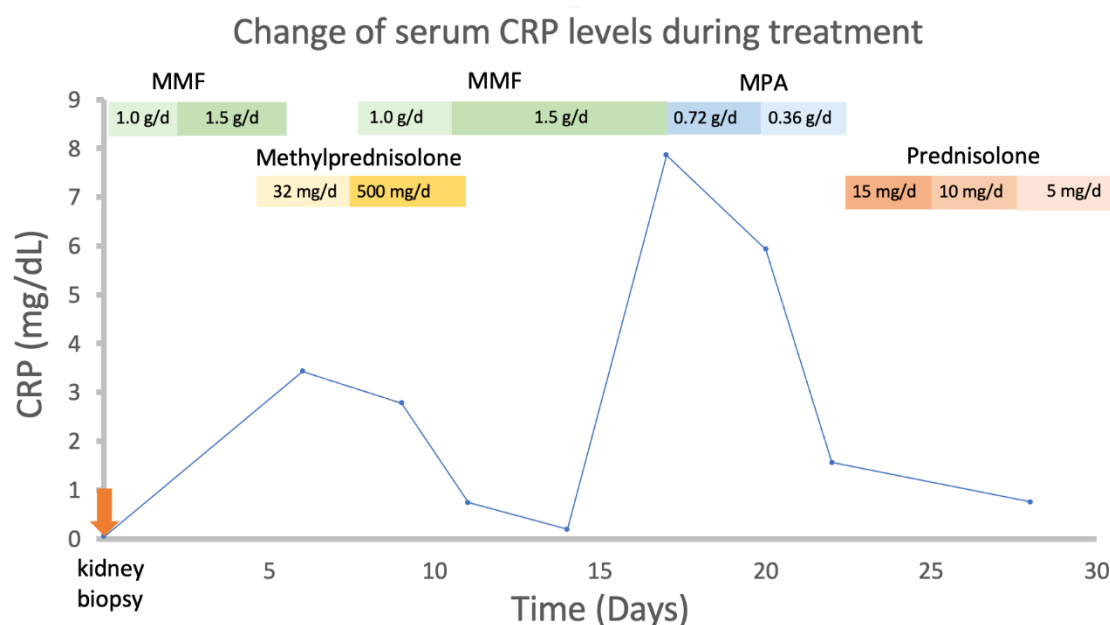


Figure 1. Clinical course illustrating CRP trends (mg/dL) and treatment interventions. Note the rapid CRP decline after MPA discontinuation.

Immunomodulatory Effects of Molecular Hydrogen Therapy in Complex Autoimmune Diseases: A Case Study on Changes in Tr1 Cells, Breg Cells, and TIM3 Expression

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Background:

Aneurysmal subarachnoid hemorrhage (SAH) complicated by autoimmune diseases presents significant therapeutic challenges, particularly when conventional treatments fail to achieve adequate disease control. Molecular hydrogen therapy has emerged as a promising adjuvant treatment modality due to its anti-inflammatory and immunomodulatory properties. This study aims to investigate the immunomodulatory effects of molecular hydrogen therapy on regulatory immune cell populations in a complex case of aneurysmal SAH with concurrent rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE).

Materials and Methods:

A 44-year-old female patient with aneurysmal SAH, pre-existing RA, and newly diagnosed SLE complicated by acute ischemic infarction was treated with daily molecular hydrogen capsules (170 mg hydrogen-rich coral calcium equivalent to 1.7×10^{21} hydrogen molecules per capsule) for six months. Comprehensive flow cytometric analysis was performed to evaluate changes in immune cell phenotypes, including T regulatory type 1 (Tr1) cells, regulatory B (Breg) cells, and TIM3 expression on cytotoxic T cells (Tc cells). Clinical parameters, autoantibody titers, and neurological assessments were monitored throughout the treatment period.

Results:

Following six months of molecular hydrogen therapy, significant improvements were observed in both clinical outcomes and immune markers. The patient demonstrated progressive neurological recovery with Glasgow Coma Scale improvement from E3M2VT to E4M6VT, and muscle strength enhancement across all limbs. Flow cytometric analysis revealed increased TIM3⁺ expression on Tc cells (baseline: 8.2% to 6-month: 15.7%), elevated Breg cell populations (baseline: 2.1% to 6-month: 4.8%), and restoration of Tr1 cell levels that correlated with clinical improvement. Anti-dsDNA antibody converted from positive to negative, and RA remained well-controlled despite discontinuation of tofacitinib. No adverse effects were reported during the treatment period.

Conclusion:

Molecular hydrogen therapy demonstrates significant potential as an adjuvant treatment for complex autoimmune conditions complicated by neurological injury. The therapy effectively modulated key regulatory immune cell populations, particularly Tr1 cells and Breg cells, while enhancing TIM3 expression on cytotoxic

T cells, suggesting improved immune tolerance and anti-inflammatory responses. These findings warrant larger-scale clinical trials to validate the therapeutic efficacy of molecular hydrogen in autoimmune diseases with neurological complications.

Diagnostic and therapeutic Challenges in Autoimmune Hemolytic Anemia with Underlying Systemic Autoimmunity and Dual Malignancies

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潛藏系統性自體免疫與雙重惡性腫瘤之自體免疫性溶血性貧血的診斷與治療挑戰

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Background:

Autoimmune hemolytic anemia (AIHA) may arise from systemic autoimmunity or malignancy. While bilirubin elevation is common, total bilirubin (T-bil) >40 mg/dL is rare and may reflect both hemolysis and biliary obstruction.

Case Presentation:

A 64-year-old woman presented with mixed-type AIHA and persistent jaundice. Workup revealed positive ANA, low complements, and antiphospholipid antibodies. She denied any other discomfort, including changes in bowel habits, vaginal spotting, weight loss, or night sweats. She received mycophenolate and belimumab for suspected systemic lupus erythematosus (SLE). She had one episode of right flank pain and admitted for further evaluation. Cecal cancer was later found and resected, with stable disease control. She developed another episode of right flank pain and marked T-bil elevation (peak at 63 mg/dL). Imaging revealed a common bile duct (CBD) stone and suspicious local recurrence of cecal cancer. Endoscopic retrograde cholangiopancreatography (ERCP) with stent placement and high-dose steroids led to rapid resolution of jaundice and hemolysis. Biopsy of a suspicious local recurrence tumor later confirmed low-grade B-cell lymphoma. Rituximab (R)-mini-CHOP chemotherapy achieved remission.

Discussion:

This case underscores the importance of recognizing dual causes of severe hyperbilirubinemia in AIHA. Timely ERCP and immunosuppression reversed both hepatic and hematologic dysfunction. The sequential discovery of two malignancies highlights the need for thorough evaluation in atypical AIHA. Multidisciplinary care was essential for a favorable outcome.

